UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/190,138	11/12/98	BOSCH H	029318/0109

HM12/0821

FOLEY & LARDNER
3000 K STREET
SUITE 500
WASHINGTON DC 20007-5109

EXAMINER	
MCQUEENEY,P	
ART UNIT	**PAPER NUMBER**
1615	8

DATE MAILED: 08/21/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/190,138	BOSCH ET AL.	
	Examiner	Art Unit	
	P. E. McQueeney	1615	

-- The MAILING DATE of this communication appears on the cov r sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *08 June 2000* .

2a)☐ This action is FINAL. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-38,40-45 and 47-58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-38,40-45 and 47-58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. Acknowledgement is made of applicant's amendment and information disclosure statement filed June 8, 2000.

2. Applicant's arguments with respect to claims 11-38, 40-45 and 47-58 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

3. Claims 11, 23, 35, 37, 40 and 42-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11, 23, 35, 37, 42 and 43 contain the phrase "poorly soluble crystalline drug." Claims 40 and 44 contain the phrase "poorly soluble drug." The phrase "poorly soluble" is indefinite because the specification lacks a standard for measuring the degree intended. Furthermore, while examiner recognizes that applicant intends this to mean "poorly water soluble," the term could also be read to mean "poorly lipid soluble" or "poorly fat soluble." This language is particularly confusing in regards to the claims in which the drug is freeze-dried. It is the position of the examiner that the freeze drying is used with components that are soluble in water, or in liquids miscible/emulsifiable with water (see Remington's p. 1565, second column, l.1-2 (aqueous solution) and Edwards et al., Example 1 (drug dissolved in methylene chloride and emulsified with water)). Examiner has not given any patentable weight to the term "poorly soluble."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

4. Claim 42 is rejected under 35 U.S.C. 102(b) as being anticipated by Adjei et al. (WO 95/27475). Adjei et al. disclose a process and apparatus for the continuous milling of aerosol pharmaceutical formulations. Adjei et al. disclose claim 42 of applicant's invention on page 1, lines 26-31.

5. Claims 11-14, 16-25, 27-33, 40, 41, 44 and 45 are rejected under 35 U.S.C. 102(e) as being anticipated by Edwards et al. (US 5,985,309). Edwards et al. disclose particles incorporating a surfactant and/or a hydrophilic or hydrophobic complex of a positively or negatively charged therapeutic agent and a charged molecule of opposite charge for drug delivery to the pulmonary system. Edwards et al. disclose claims 11-14 and 16-22 of the present invention in claims 1-12; col. 4, l. 66-67; col. 5, l. 1-67; col. 6, l. 1-67; col. 7, l. 1-67; col. 8, l. 1-67; col. 9, l. 1-29; col. 11, l. 62-67; col. 12, l. 1-67; col. 13, l. 1-47; and Examples 2 and 4-14.

Edwards et al. disclose claims 23-25 and 27-33 of the present invention

in claims 1-12; col. 4, l. 66-67; col. 5, l. 1-67; col. 6, l. 1-67; col. 7, l. 1-67; col. 8, l. 1-67; col. 9, l. 1-29; col. 11, l. 62-67; col. 12, l. 1-67; col. 13, l. 1-47; and Example 1.

Edwards et al. disclose claims 40 and 41 of the present invention in Examples 5-14. Edwards et al. disclose claims 44 and 45 of the present invention in Example 1.

6. Claims 37, 38 and 50 are rejected under 35 U.S.C. 102(e) as being anticipated by Wiedmann et al. (US 5,747,001). Wiedmann et al. disclose an aerosol comprising droplets of an aqueous dispersion of nanoparticles, said nanoparticles comprising insoluble beclomethazone particles having a surface modifier on the surface thereof. Wiedmann et al. disclose claims 37 and 38 in the abstract; claims 1 and 2; col. 2, l. 60-65; col. 3, l. 5-67; col. 4, l. 1-67; col. 5, l. 1-64; col. 10, l. 15-52; and Example 1. Wiedmann et al. disclose claim 50 of the present invention in Example 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. Claims 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adjei et al. as discussed above and Liversidge et al. (EP 0 499 299). Adjei et al. do not disclose the pressurized conditions of applicant's claim 43. Liversidge et al. disclose at page 5, lines 46-51 that ambient pressures are typical of ball mills, attritor mills and vibratory mills and that processing pressures of up to about 20 psi are typical of media milling. It is the position of the examiner that one skilled in the art would be able to determine the best method to product nanoparticles suitable for inhalation, whether by spray-drying, freeze drying, pressurized or non-pressurized milling. The expected result would be smaller particles as compared to the originating material that are suitable for inhalation.

8. Claims 11-34, 40, 41, 44, 45, 47, 48 and 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards et al. as discussed above.

Edwards et al. do not disclose the particle size of the active substance (claims 15, 26 and 51-58). It is the position of the examiner that Edwards et al. meets applicant's particle size limitations because Edwards et al. discloses powders comprised of active and additional excipients when combined yield a product size of 1-3 microns (see claim 2).

Furthermore, even if Edwards et al. do not include particles of applicant's claim limitation, this limitation is therefore not granted any patentable weight. If Edwards et al.

can start with larger particles and yield applicant's instant invention, then applicant's limitation is merely superfluous.

Edwards et al. do not combine a freeze-dried drug with a spray dried drug (claim 34). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to combine two or more medicaments (i.e., Combivent® (ipratropium bromide and albuterol sulfate)) to form a multipurpose dosage form. The expected result would be a single route of administration that treats multiple symptoms.

Edwards et al. do not prescribe a dosing regimen (claims 47 and 48). It is the position of the examiner that the dosage concentration would routinely be determined by one of ordinary skill in the art. Furthermore, this concentration will vary from medicament to medicament. Finally, it is the position of the examiner that the duration of delivery time for aerosol administration is definitely less than 15 seconds for all inhalers. Examiner is unaware of any human beings who can inhale for longer than 15 seconds.

9. Claims 11-36, 40, 41, 44, 45, 47-49 and 51-58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Edwards et al. as discussed above in combination with Smith et al. (US 5,785,049).

Edwards et al. do not disclose their propellant. Smith et al. disclose an apparatus for dispersion of dry powder medicaments. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the apparatus of Smith et al. with the medicaments of Edwards et al. in order to provide a method to

aerosolize the dry powder of Edwards et al. The expected result would be effective delivery of the dry powder medicaments of Edwards et al.

10. Claims 37, 38 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wiedmann et al. Wiedmann et al. do not disclose the duration of the delivery time of their aerosol formulation. As stated above, it is the position of the examiner that this time is definitely less than 15 seconds for all inhalers.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. E. McQueeney whose telephone number is 703-306-5827. The examiner can normally be reached on weekdays from 8:30 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page, can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600